The Impact of Influenza Epidemics on Mortality: Introducing a Severity Index

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ABSTRACT

Objectives. The purpose of this study was to assess the impact of recent influenza epidemics on mortality in the United States and to develop an index for comparing the severity of individual epidemics.

Methods. A cyclical regression model was applied to weekly national vital statistics from 1972 through 1992 to estimate excesses in pneumonia and influenza mortality and all-cause mortality for each influenza season. Each season was categorized on the basis of increments of 2000 pneumonia and influenza excess deaths, and each of these severity categories was correlated with a range of all-cause excess mortality.

Results. Each of the 20 influenza seasons studied was associated with an average of 5600 pneumonia and influenza excess deaths (range, 0–11 800) and 21 300 all-cause excess deaths (range, 0–47 200). Most influenza A(H3N2) seasons fell into severity categories 4 to 6 (23 000–45 000 all-cause excess deaths), whereas most A(H1N1) and B seasons were ranked in categories 1 to 3 (0–23 000 such deaths).

Conclusions. From 1972 through 1992, influenza epidemics accounted for a total of 426 000 deaths in the United States, many times more than those associated with recent pandemics. The influenza epidemic severity index was useful for categorizing severity and provided improved seasonal estimates of the total number of influenza-related deaths. (*Am J Public Health.* 1997;87:1944–1950)

Introduction

Assessing the burden of influenza epidemics on mortality is difficult. Influenza diagnoses are generally not laboratory confirmed, and deaths related to influenza are often attributed to pneumonia and other secondary complications that occur well after the influenza virus infection.[1] For these reasons, influenza may not be listed on the death certificate for many influenza-related deaths.

Given this incomplete identification, an indirect approach involving statistical modeling has long been used to estimate the seasonal excess in mortality attributable to influenza. Excess mortality during an influenza season is calculated as the difference between the number of deaths observed and the expected baseline in the absence of influenza.[2–11]

The excess mortality approach is justified by numerous observations of increased mortality during influenza epidemics that is attributed to pneumonia and preexisting chronic lung, heart, and kidney conditions.[1,2] The primary index for assessing the severity of influenza epidemics has long been based on national levels of pneumonia- and influenza-related deaths. However, pneumonia and influenza excess mortality estimates account for only a subset of influenza-associated deaths and are not a good measure of the total burden of influenza on mortality. Another measure, the excess in mortality due to any cause of death (all-cause excess mortality), potentially captures all influenza-related deaths, but these seasonal estimates may not be as accurate as pneumonia and influenza excess mortality estimates.

Lui and Kendal provided excess mortality estimates for the influenza seasons in the United States from 1972 through 1985.[11] To provide more current estimates, we modified Lui and Kendal's cyclical regression model approach and applied our model to weekly vital statistics for 1972 through 1992. In this paper we report on pneumonia and influenza and all-cause excess mortality for the 20 influenza seasons during this period and use these results to demonstrate the difference in the impact on mortality of the three currently circulating types and subtypes of influenza viruses: A(H3N2), A(H1N1), and B. We have also developed an influenza epidemic severity index that both compares the relative severity of each season and provides reliable seasonal estimates of the total impact of influenza on mortality.

Methods

Data Sources

Multiple-cause-of-death data for the United States from 1972 through 1992 were obtained from the National Center for Health Statistics (NCHS).[12] Classifications for cause of death were based on the *International Classification of Diseases*, eighth revision, adapted (ICDA-8), and ninth revision (ICD-9).[13,14] To ensure comparability

with previous reports of pneumonia and influenza excess mortality,[10,11] a pneumonia or influenza death was defined as a death with one of the following codes listed as the single underlying cause of death: ICDA-8 codes 480 through 486 (pneumonia of viral, bacterial, and unknown cause) and 470 through 474 (influenza) for the years 1972 through 1978, and the comparable ICD-9 codes 480 through 487 for the years 1979 through 1992. An all-cause death was defined as a death due to any cause.

The Model

A cyclical regression model approach was developed and applied to the pneumonia and influenza and all-cause mortality data. (The specific approach and the underlying assumptions are presented in an appendix available from the authors.) Our model is a revised version of Lui and Kendal's model,[11] designed for weekly instead of monthly mortality data. The baseline of mortality in the absence of influenza-associated deaths was established by fitting the regression model for successive 5-year data periods after excluding epidemic weeks. After fitting the model to data from the first 5-year period, the baseline was computed as the model forecast for the subsequent year (Figure 1).

The model identified epidemic periods as those weeks during each influenza season (October through May, or weeks 40 through 52 or 53 and 1 through 20) when the observed number of deaths exceeded the epidemic threshold (defined as the upper 95% confidence limit on the baseline) for 2 or more consecutive weeks. By definition, the epidemic periods ended whenever the observed number of deaths declined below this epidemic threshold for 2 or more consecutive weeks. The timing of these model-identified epidemic periods was compared with the timing of influenza epidemics defined by increased numbers of influenza virus isolations in the United States reported to the Centers for Disease Control (CDC) by World Health Organization collaborating laboratories (CDC, unpublished data).

Excess Mortality

For each influenza season, the excess pneumonia and influenza mortality was estimated as the difference between the observed and baseline numbers of pneumonia- and influenza-related deaths during the model-identified epidemic periods. All-cause excess mortality estimates were obtained by applying the model to weekly
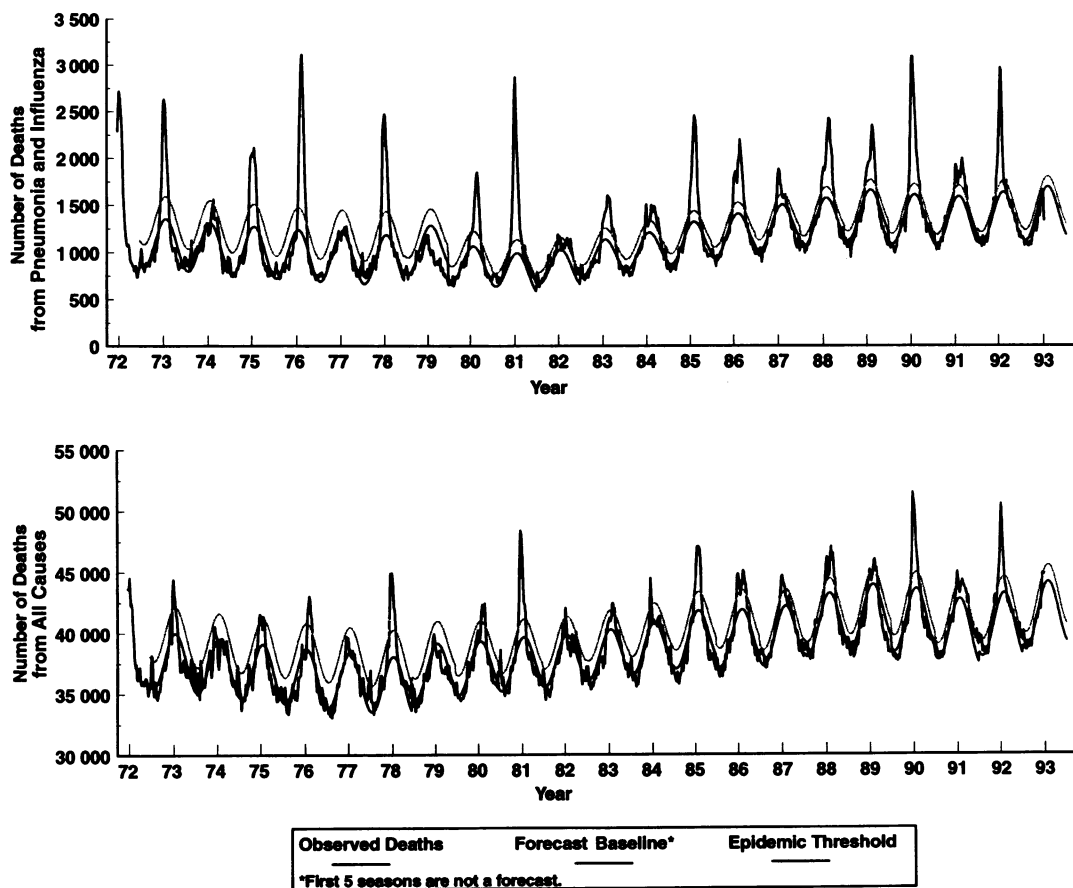
Note. The model-derived baselines and upper epidemic threshold are indicated as sinusoidal lines.

Figure 1—Number of deaths with pneumonia or influenza as the underlying cause (top) and number of deaths from all causes (bottom), by week, for the period January 1972 through December 1992.

numbers of deaths due to any cause. Because the model-identified epidemic periods for the latter were significantly shorter than those based on pneumonia and influenza mortality data as well as laboratory-confirmed influenza virus activity, we included excess deaths during the 4 weeks (2 weeks on each side) surrounding the identified epidemic period for all-cause mortality data.[11]

The upper and lower 95% confidence limits on the baseline were used to calculate the lower and upper uncertainty limits, respectively, for seasonal excess mortality estimates.

Influenza Epidemic Severity Index

Pairs of pneumonia and influenza and all-cause excess deaths for the 20 seasons studied were plotted and the regression line was fitted through the origin by the restricted least squares method.[15] Each severity category was defined as a range of 2000 pneumonia and influenza excess deaths, starting at 0 deaths (x-axis). To compute a range of total influenza-associated deaths for each category, the regression line was used to correlate each category limit of pneumonia and influenza deaths with the corresponding number of all-cause deaths (y-axis). Previously published pneumonia and influenza and all-cause excess mortality estimates for the pandemics of 1957/58 and 1968/69[1] were used to indicate the fit of these data with the correlation based on the 20 studied nonpandemic seasons and to place the pandemics in the severity index.

Results

The Model

The sinusoidal regression model we applied to weekly pneumonia and influenza as well as all-cause mortality data is of the following form: $Y_t = a + b*t + c*t^2 + d*\cos(2*t*\Pi \div 52.1667) + f*\sin(2*t*\Pi \div 52.1667) + e_t$. Where Y_t is the estimated mortality for week t; t is the index for week of death (t = 1,2,...,1043); a is the intercept on the Y_t axis; b is the linear (secular) trend in pneumonia and influenza deaths; c is the quadratic coefficient indicating deviation from the linear trend; d and f are harmonic coefficients indicating seasonality; e_t is error; and 52.1667 is the mean number of weeks per year adjusted for extra days in leap years. This regression model provided a good fit to both the pneumonia and influenza and the all-cause mortality data

after excluding the epidemic weeks (R^2 ranged from 0.71 for the first regression cycle to R^2 values higher than 0.88 for the last two 5-year regression cycles). Autocorrelation of the residuals e_t could not be reduced by adding additional sine and cosine terms, but was elevated somewhat by removing the quadratic term $c*t^2$.

The timing of the epidemic periods identified when applying the model to pneumonia and influenza mortality data was consistent with the timing of periods with documented influenza virus activity. All weeks with increased laboratory-confirmed influenza virus activity occurred between week 49 and week 9 (December to March). For 11 of the 17 seasons with excess pneumonia and influenza mortality detected, the epidemic periods occurred simultaneously with or within 4 weeks after the period of increased laboratory-confirmed influenza. For the remaining seasons, a total of 13 weeks of the identified epidemic periods occurred either before or later than 5 weeks after the periods in which increased influenza virus activity was documented.

For the 17 seasons with excess pneumonia and influenza mortality, the model identified a mean of 12.5 epidemic weeks per season (range 6 to 18 weeks). For the 16 seasons with excess all-cause mortality, the model identified a mean of 7.1 epidemic weeks (range 2 to 13 weeks) per season.

During influenza seasons with excess mortality, the percentage increase above the baseline level was substantially greater for pneumonia and influenza deaths than for all-cause deaths. For example, during the peak week of the severe 1975/76 influenza A(H3N2) season, the observed number of pneumonia and influenza deaths was 157% greater than the baseline level, whereas the number of all-cause deaths was only 12% greater than the baseline level.

Pneumonia and Influenza Excess Mortality

For the 20 influenza seasons studied, we estimated an average of 5600 pneumonia and influenza excess deaths per season (range, 0 to 11 800 deaths) (Table 1). Three seasons (1973/74, 1976/77, and 1978/79) were not associated with measurable excess pneumonia and influenza mortality. The 3 most severe seasons, 1975/76, 1980/81, and 1989/90, were characterized by a predominance of influenza A(H3N2) viruses and were associated with more than 10 000 pneumonia and influenza excess deaths. For the 11 seasons in which influenza type A(H3N2) circulated, we

estimated an average of 7600 excess pneumonia and influenza deaths. In contrast, for the 9 seasons in which influenza B viruses, influenza A(H1N1) viruses, or both, predominated, we estimated an average of 3200 pneumonia and influenza excess deaths per season.

For the seasons from 1972 through 1985 for which data were available from Lui and Kendal[11] or Choi and Thacker,[10] these authors' estimates of pneumonia and influenza excess deaths were within the uncertainty limits of our estimates, with a few exceptions (Table 1). A maximum discrepancy on the estimates of 3200 pneumonia and influenza deaths was obtained for the 1983/84 season, and, although we estimated 2100 ± 1500 pneumonia and influenza excess deaths for the 1981/82 season, Lui and Kendal reported no excess mortality for this season. Our estimates of pneumonia and influenza excess deaths were on average 3% higher (range, −47% to +28%) than those of Lui and Kendal and 14% higher (range, −4% to +31%) than those of Choi and Thacker.

All-Cause Excess Mortality

When the model was applied to all-cause deaths in the United States, all-cause excess mortality was estimated to be 21 300 excess deaths on average per season (range, 0 to 46 200 deaths) (Table 1). Thus, the total burden of influenza on mortality during the 20 nonpandemic influenza seasons studied was 426 000 all-cause excess deaths. For the seasons 1973/74, 1976/77, 1978/79, and 1981/82, no excess mortality was detected. The seasonal number of all-cause excess deaths was on average 3.8 times larger than the number of pneumonia and influenza excess deaths.

The uncertainty intervals on our estimates of all-cause excess mortality were large; for several seasons, the uncertainty interval was ± 20 000 deaths. On average, the inclusion of 4 weeks surrounding the identified epidemic periods increased our estimates of all-cause excess mortality by 3000 per season. Comparisons of our all-cause excess mortality estimates with those of Lui and Kendal[11] and Choi and Thacker[10] showed that (with one exception) these authors' estimates were within the uncertainty limits of our estimates, but that there were discrepancies of as many as 22 000 deaths for some seasons (Table 1). Our all-cause excess estimates were on average 2% higher (range, −49% to 98%) than those of Lui and Kendal and 35% higher (range, −37% to 101%) than those of Choi and Thacker.

TABLE 1—Pneumonia- and Influenza-Related and All-Cause Excess Mortality Estimates for 20 Influenza Seasons: United States, 1972 through 1992

Season	Predominant Strain(s)[a]	Pneumonia and Influenza Excess Deaths (range)[b]	Pneumonia and Influenza Excess Deaths, Other Studies	All-Cause Excess Deaths (range)[b]	All-Cause Excess Deaths, Other Studies
1972/73	A/England/42/72(H3N2)	7900 (5500–10 300)	6 300[c] 7 300[d]	18 300 (1200–35 000)	21 400[c] 29 200[d]
1973/74	B/HongKong/72	0	0[c]	0	0[c]
1974/75	A/Port Chalmers/1/73(H3N2)	6500 (4100–8900)	5 100[c] 5 600[d]	15 100 (0–32 100)	7 600[c] 7 500[d]
1975/76	A/Victoria/3/75(H3N2)	11 800 (9200–14 400)	11 000[c] 10 600[d]	24 600 (3400–45 900)	28 200[c] 28 700[d]
1976/77	A/Victoria/3/75 (H3N2) B/HongKong/72	0	0[c]	0	0[c]
1977/78	A/Texas/1/77(H3N2) A/USSR/77(H1N1)	8300 (6000–10 500)	8 700[c] 6 900[d]	46 200 (19 800–72 700)	53 000[c] 24 000[d]
1978/79	A/Brazil/78(H1N1)	0	0[c]	0	0[c]
1979/80	B/Singapore/222/79	5100 (3500–6700)	4 900[c] 4 600[d]	17 300 (600–34 100)	34 200[c]
1980/81	A/Bangkok/1/79(H3N2)	11 700 (9100–14 200)	9 900[c] 7 800[d]	47 200 (27 800–66 600)	46 500[c]
1981/82	B/Singapore/222/79 A/England/333/80(H1N1)	2100 (600–3700)	0[c]	0	
1982/83	A/Bangkok/1/79(H3N2)	4700 (2800–6700)	4 000[c]	9 600 (0–19 200)	
1983/84	B/USSR/100/83 A/Chile(H1N1)	3500 (1600–5400)	6 700[c]	8 200 (0–17 600)	
1984/85	A/Mississippi/85(H3N2) A/Philippines/82(H3N2)	8100 (6600–9600)	10 900[c]	36 200 (17 700–54 700)	
1985/86	B/AnnArbor/86	6700 (4900–8500)		34 000 (6800–61 200)	
1986/87	A/Taiwan/86/(H1N1)	1800 (1100–2500)		16 800 (1900–31 700)	
1987/88	A/Sichuan/87(H3N2)	7400 (5600–9100)		33 400 (12 900–53 800)	
1988/89	B/Victoria/87 A/Taiwan/86(H1N1)	5100 (3600–6600]		10 500 (800–20 200)	
1989/90	A/England/88(H3N2)	10 100 (8500–11 700)		43 600 (27 600–59 600)	
1990/91	B/Panama/90	4200 (2400–6100)		23 000 (0–46 000)	
1991/92	A/Beijing/89(H3N2)	6600 (5600–7700)		41 700 (19 600–63 700)	

[a]From Noble[1] for 1972/73 through 1978/79; later years based on US surveillance for circulating strains (Centers for Disease Control and Prevention, unpublished data).
[b]The range is based on the upper and lower uncertainty limit on the excess mortality estimate, calculated as the excess deaths above the 95% lower and upper confidence limits on the model-derived baseline.
[c]Based on Lui and Kendal's cyclical regression model for monthly vital statistics.[11] Estimates listed are the means of their calculated ranges.
[d]Based on Choi and Thacker's autoregressive integrated moving average model for monthly vital statistics.[10]

Influenza Epidemic Severity Index

We observed a linear correlation ($R^2 = .67$) between the estimates of pneumonia and influenza and all-cause excess deaths for the 20 seasons studied (Figure 2). The 10 severity categories of the influenza epidemic severity index and their corresponding ranges of influenza-associated deaths are presented in Table 2. For each severity category, a corresponding range of all-cause excess deaths was computed on the basis of the observed relationship between pneumonia and influenza excess mortality and all-cause excess mortality for the 20 seasons studied. Because the seasonal pneumonia and influenza excess mortality estimates
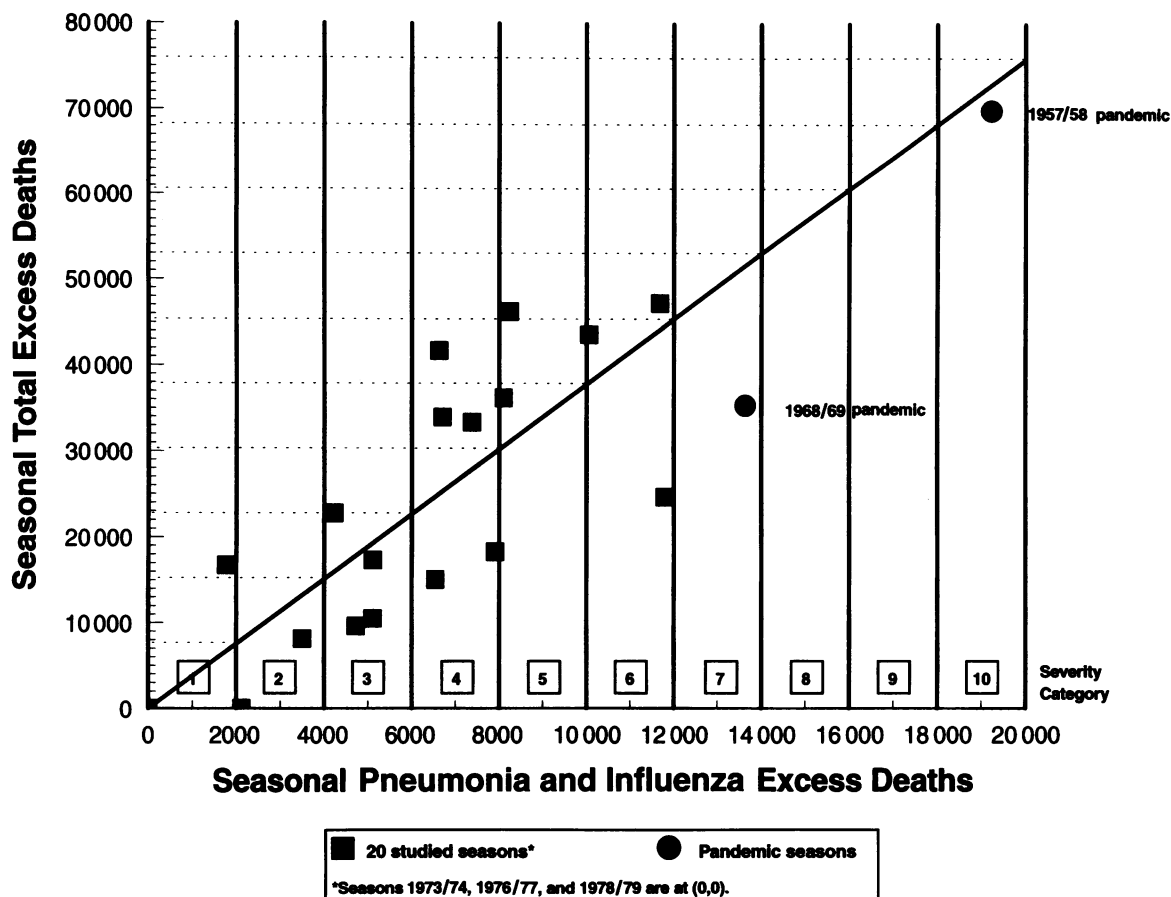
ranged from 0 to 11 800 deaths, none of the 20 seasons ranked higher than severity category 6 (corresponding to a range of 38 000 to 45 000 all-cause excess deaths).

Most seasons in which influenza A(H3N2) viruses predominated fell into categories 4, 5, or 6 (corresponding to 23 000 to 45 000 all-cause excess deaths), while most seasons in which influenza B or A(H1N1), or both, predominated fell into categories 1, 2, or 3 (corresponding to 0 to 23 000 all-cause excess deaths). The two seasons when only influenza A(H1N1) viruses were circulating (1978/79 and 1986/87) were classified as severity category 1 (0 to 8000 total influenza-associated deaths).

On the basis of previously reported estimates of pneumonia and influenza excess mortality,[1] the pandemic of 1957/58 was classified as severity category 10 (corresponding to 68 000 to 76 000 all-cause deaths) and the pandemic of 1968/69 as severity category 7 (corresponding to 45 000 to 53 000 all-cause deaths).

Discussion

The use of national mortality data and statistical models to quantify influenza-associated mortality has been an important epidemiological tool since the concept was introduced by William Farr in his reports of

TABLE 2—The Influenza Epidemic Severity Index

Category	Range of Pneumonia and Influenza Excess Deaths	Range of Total Influenza-Associated Deaths[a]	Influenza Seasons 1972 to 1997[b] and Two Most Recent Pandemics
1 (Mild)	0– 2 000	0– 8 000	1973/74, 1976/77, 1978/79, 1986/87, 1995/96[b]
2	2 000– 4 000	8 000– 15 000	1981/82, 1983/84
3	4 000– 6 000	15 000– 23 000	1979/80, 1982/83, 1988/89, 1990/91, 1994/95, 1996/97[b]
4	6 000– 8 000	23 000– 30 000	1972/73, 1974/75, 1985/86, 1987/88, 1991/92, 1992/93
5	8 000– 10 000	30 000– 38 000	1977/78, 1984/85, 1993/94
6	10 000– 12 000	38 000– 45 000	1975/76, 1980/81, 1989/90
7	12 000– 14 000	45 000– 53 000	1968/69 pandemic[c]
8	14 000– 16 000	53 000– 60 000	
9	16 000– 18 000	60 000– 68 000	
10 (Severe)	18 000– 20 000	68 000– 76 000	1957/58 pandemic[c]

[a]The range of total influenza-associated deaths for each severity category is based on the correlation between all-cause excess deaths and pneumonia and influenza excess deaths for 20 interpandemic influenza seasons studied.

[b]The severity category for the seasons 1992/93, 1993/94, and 1994/95 were based on newly available national vital statistics from NCHS, while the severity categories indicated for 1995/96 and 1996/97 are preliminary and based on analysis of mortality data from CDCs 121 Cities surveillance system.[20]

[c]The two pandemic seasons were categorized on the basis of previously published pneumonia and influenza excess estimates.[1]

model approach that accounted for autocorrelation in the data,[10] it appears that there is a robustness in the data for producing similar results regardless of the modeling approach.

Determination of all-cause excess mortality from national vital statistics data has contributed the best available measure of the total burden of influenza epidemics on mortality. However, we found that individual seasonal all-cause excess mortality estimates lacked precision, because the occurrence of influenza-associated deaths only marginally affected the weekly numbers of deaths due to any cause. This lack of precision was evident in the broad uncertainty intervals and in the occasional wide disparities between our all-cause excess mortality estimates and those of other investigators.[10,11] Some of the discrepancies between our estimates and those of Choi and Thacker[10] may be explained by the different modeling approaches, including the exclusion, vs replacement, of deaths during epidemic weeks when fitting the model.

To provide a method to better compare the relative severity and to provide more reliable estimates of the total mortality burden of influenza epidemics, we developed the influenza epidemic severity index. We used the relative precision of the pneumonia and influenza excess mortality estimates to rank influenza epidemics into severity categories and provided a range of all-cause excess mortality for each category, based on the observed linear relationship between pneumonia and influenza excess mortality and all-cause excess mortality for the 20 influenza seasons studied. The influenza seasons during the period 1972 through 1992 ranked as categories 1 (mild) through 6 (severe). The severity varied with circulating influenza virus type and subtype: most seasons dominated by influenza A(H3N2) viruses were classified in category 4, 5, or 6 on the severity index (corresponding to 23 000 to 45 000 all-cause excess deaths), while seasons in which influenza B and A(H1N1) viruses circulated were typically associated with little excess mortality and ranked in category 1, 2, or 3 (corresponding to 0 to 23 000 all-cause excess deaths). On the basis of previously reported pneumonia and influenza excess mortality estimates,[1] the 1957/58 A(H2N2) pandemic and the 1968/69 A(H3N2) pandemic fell into category 10 (68 000 to 76 000 all-cause excess deaths) and category 7 (45 000 to 53 000 all-cause excess deaths), respectively, consistent with the general observation that pandemics are particularly severe.

Cumulatively, the 20 nonpandemic influenza seasons studied accounted for 426 000 related deaths, manyfold more deaths than were attributed to the two recent pandemics. Thus, this study also emphasizes the important contribution of regular nonpandemic influenza seasons to overall influenza-associated mortality.

While this manuscript has been in preparation, more recent national vital statistics data have been made available from NCHS and a recently developed method now allows a preliminary assessment of the severity immediately after each influenza season using mortality surveillance data.[20] We have therefore indicated in Table 2 the severity index categories for the five most recent influenza epidemics during the period 1992 to 1997.

The impact of future influenza epidemics in the United States may be determined and reported solely on the basis of the seasonal pneumonia and influenza excess mortality estimates that provide a ranking in the influenza epidemic severity category. An assessment of the total burden of influenza on mortality will then be provided by the index as the corresponding range of all-cause excess deaths, replacing the traditional reporting of seasonal all-cause excess mortality estimates that are associated with very large uncertainty limits. □

References

1. Noble GR. Epidemiological and clinical aspects of influenza. In: Beare AS, ed. *Basic and Applied Influenza Research*. Boca Raton, Fla: CRC Press; 1982:11–50.
2. Housworth J, Langmuir AD. Excess mortality from epidemic influenza, 1957–1966. *Am J Epidemiol*. 1974;100:40–48.
3. Collins SD. Excess mortality from causes other than influenza and pneumonia during influenza epidemics. *Public Health Rep*. 1932;47:2159–2181.
4. Collins SD, Lehmann J. Trends and epidemics of influenza and pneumonia, 1918–1951. *Public Health Rep*. 1951;66:1487–1516.

5. Eickhoff TC, Sherman IL, Serfling RE. Observations on excess mortality associated with epidemic influenza. *JAMA.* 1961;176:776–782.

6. Stroup DF, Thacker SB, Herndon JL. Application of multiple time series analysis to the estimation of pneumonia and influenza mortality by age, 1962–1983. *Stat Med.*1988; 7:1045–1059.

7. Serfling RE. Methods for current statistical analysis of excess pneumonia-influenza deaths. *Public Health Rep.* 1963;78:494–506.

8. Alling DW, Blackwelder WC, Stuart-Harris CH. A study of excess mortality during influenza epidemics in the United States, 1968–1976. *Am J Epidemiol.* 1981;113: 30–43.

9. Choi K, Thacker SB. An evaluation of influenza mortality surveillance, 1962–1979. *Am J Epidemiol.* 1981;113:215–226.

10. Choi K, Thacker SB. Mortality during influenza epidemics in the United States, 1967–1978. *Am J Public Health.* 1982;72:1280–1283.

11. Lui K-J, Kendal AP. Impact of influenza epidemics on mortality in the United States from October 1972 to May 1985. *Am J Public Health.* 1987;77:712–716.

12. *Vital Statistics Mortality Data, Multiple Cause Detail, 1969–1991.* Public use data tape contents and documentation package. Hyattsville, Md: National Center for Health Statistics; 1992.

13. World Health Organization. *International Classification of Diseases, Eighth Revision, Adapted for Use in the United States.* Washington, DC: US Government Printing Office; 1975.

14. *Manual of the International Statistical Classification of Diseases, Injuries, and Causes of Death.* Based on recommendations of the Ninth Revision Conference, 1975, and adopted by the Twenty-Ninth World Health Assembly. Geneva, Switzerland: World Health Organization; 1977.

15. Freund RJ, Littell RC. *SAS System for Regression.* 2nd ed. Cary, NC: SAS Institute Inc; 1991;210:41–42.

16. Humphrey N, ed. *Vital Statistics: Memorial Volume of Selections from the Writings of William Farr.* Part 4. London, England: Sanitary Institute of Great Britain; 1885:330.

17. Glezen P, Ardath AP, Snyder DN, Downs TD. Mortality and influenza. *J Infect Dis.* 1982;146:313–321.

18. Barker WH, Mullooly JP. Underestimation of the role of pneumonia and influenza in causing excess mortality. *Am J Public Health.* 1981;71:643–645.

19. *Instructions for Classifying the Underlying Cause of Death.* Hyattsville, Md: National Center for Health Statistics; 1992.

20. Simonsen L, Clarke MJ, Stroup DF, Williamson GD, Arden NC, Cox NJ. A method for timely assessment of influenza-associated mortality in the United States. *Epidemiol.* 1997;8:390–395.